In Brief

Cancer screening is widely assumed to be an effective means of reducing cancer-related mortality. Yet, recommendations on cancer screening should always be based on evidence and not assumptions. Over the years, numerous studies were undertaken to determine the efficacy of screening, including case-control, retrospective, and prospective studies. However, there are 3 biases pertinent to many of these studies: lead time, length, and selection. Lead-time bias refers to the interval of time between diagnosis of cancer by screening and usual clinical detection. Lead-time bias may lead one to erroneously believe that screening prolongs life, when it simply extends the period of time over which the cancer is observed. Length bias refers to the fact that slower growing tumors exist for a longer period in the preclinical phase and are more likely to be detected by screening. By contrast, the faster growing tumors (more aggressive cancers) exist for a shorter period of time in the preclinical phase and are more likely to be detected in the intervals between screening sessions (as symptomatic cases). Finally, studies comparing volunteers for cancer screening with nonvolunteer controls are subject to a selection bias. Thus, the lower mortality rate for individuals who undergo cancer screening might not be due entirely to screening, but also partly to other factors associated with healthy volunteers. In light of these 3 biases, the best way to determine the efficacy of screening is to undertake large, randomized prospective trials, with mortality as the endpoint.

For cervical, prostate, ovarian, lung, breast, and colorectal cancers, there has been considerable interest in screening as a means of reducing cancer-related mortality. However, evidence of benefit from randomized prospective trials is often lacking. For cervical cancer, national mortality data seem to support the notion that screening with the Papanicolaou test can effectively reduce mortality, but there are no data from randomized clinical trials. Prostate cancer screening is undertaken with digital rectal examination and measurement of serum prostate specific antigen (PSA). Although it is widely practiced in the United States, there are no data from well-designed trials to show whether or not prostate cancer screening has

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any impact on mortality. However, trials are in progress. Ovarian cancer screening has been undertaken with transvaginal ultrasound, measurement of CA-125, or adnexal palpation. Many experts believe that screening for ovarian cancer is not indicated for women at normal risk but might be useful for those with a genetic predisposition. Yet, evidence from clinical trials is lacking. Lung cancer screening has been evaluated in 4 randomized trials undertaken in the 1970s. The Memorial Sloan-Kettering and Johns Hopkins trials examined the value of screening with sputum cytology, and the Mayo Clinic and Czech trials examined the efficacy of screening with both sputum cytology and chest radiography. In all of these trials, screening was found to have no impact on lung cancer mortality. Yet, considerable interest in screening for lung cancer remains, and spiral computed tomography (CT) is undergoing evaluation in clinical trials.

There are 3 methods of screening for breast cancer that are widely used today: mammography, clinical breast examination (CBE) by trained personnel, and breast self-examination (BSE). Recently, attention has also turned to screening with magnetic resonance imaging (MRI), particularly for younger women at high risk for developing breast cancer, but there are no data from randomized trials concerning its impact on breast cancer mortality.

Eight randomized prospective trials have examined the efficacy of mammography screening: the Health Insurance Plan (HIP) trial of New York, Swedish Two County, Goteborg, Stockholm, Malmo, Edinburgh, the Canadian National Breast Screening Study I (CNBSS I), and CNBSS II. Meta-analyses of these trials indicate that mammography screening can effectively reduce breast cancer mortality, but the benefit is more clearly established in women older than the age of 50. Four of these trials have also included CBE, and one might interpret the results to indicate that CBE is also an effective screening modality. A trial to determine the efficacy of screening with CBE alone is currently under way in India, but the results will not be available for several more years. Two large randomized controlled trials have examined the efficacy of screening with BSE. The first of these was undertaken under the auspices of the World Health Organization in Leningrad (now St. Petersburg), Russia, and another was conducted in Shanghai, China. These trials have not demonstrated any mortality benefit to screening with BSE. The various harmful effects of breast cancer screening should also be considered: lead time, false-positives, overdiagnosis, exposure to low dose radiation, and costs.

The efficacy of screening for colorectal cancer has been evaluated in 4 large randomized prospective trials: Minnesota, Nottingham (UK), Funen

(Denmark), and Goteborg (Sweden). These trials showed that fecal occult blood testing (FOBT) can effectively reduce mortality from colorectal cancer by approximately 20%. However, there is now considerable controversy as to what constitutes the optimal screening strategy for colorectal cancer. Several novel screening modalities have been introduced in recent years. Options for colorectal screening include DNA-based stool test, double contrast barium enema (DCBE), virtual colonoscopy, flexible sigmoidoscopy, and colonoscopy. For many valid reasons, it may not be necessary or even practical to screen all average risk individuals with the current "gold" standard, screening colonoscopy. A tiered or layered approach based on a better understanding of the genetic and environmental components of colorectal cancer might be more appropriate, with lower risk individuals receiving the least intensive and least invasive procedures, and higher risk individuals having the more intensive procedures.

All individuals considered for cancer screening should be informed of its risks and benefits. This is especially true in circumstances in which the efficacy of screening has not been fully established or is controversial, such as mammography screening for women younger than age 50 or screening with colonoscopy (rather than FOBT). It is important to keep in mind that cancer screening targets asymptomatic individuals, and obtaining informed consent before screening provides a good opportunity for discussing its risks and benefits.